

AIChE 2008 Annual Meeting

Abstract

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Lasentec FBRM IPC-PAT method development and validation for wet milling process

Lasentec FBRM in-situ measurement is used to monitor particle size in many different operations such as crystallization and wet milling. It can be installed in recirculation loops, or directly in vessels of different sizes ranging from 50 mL to thousands of gallons. Despite the popularity of the technique, it has never been used as an In-Process-Control (IPC) tool in the pharmaceutical industry. Its common use is to understand and troubleshoot processes or what is generally termed “information gathering”. One reason that the FBRM technique has not been used as an IPC or “release” test is the higher probability of variable results. The variation normally encountered is due to difficulties in controlling operating conditions to the level that is possible for off-line tests. However, there is evident advantage to the use of in-line process analytical techniques (PAT) such as Lasentec FBRM to speed up and streamline API manufacturing and potentially allow superior process control which is not possible with traditional off-line measurements.

This presentation describes efforts towards developing and validating the Lasentec FBRM as an IPC method for a wet milling process of an active pharmaceutical ingredient (API). Results from a pilot plant campaign suggest up to 10% variation with different flow rates in the recirculation loop in which the Lasentec probe was placed. Additional laboratory scale studies reveal other contributing factors to variability when the Lasentec probe is installed in the crystallizer - rpm of the agitator, location of the probe, and scanning speed of the laser. Results from the robustness studies will be discussed in this presentation.

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